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EXAMINER	
RAILEY, J	
ART UNIT	PAPER NUMBER
1636	17

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Please find ~~below~~ attached a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Office Action Summary	Application No. 08/485,943	Applicant(s) Friedman et al.
	Examiner J. Railey	Group Art Unit 1636

☒ Responsive to communication(s) filed on *27 Mar 1998*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *54-162* is/are pending in the application.

Of the above, claim(s) *54-123 and 125-131* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *124 and 132-162* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *14*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636.

The specification contains nucleotide sequences which lack SEQ ID numbers at page 142, line 29 and page 143, line 6. It appears that these two oligonucleotides are found as SEQ ID NOs: 63 and 64, respectively. If this is indeed the case, applicant should indicate these oligonucleotides by (SEQ ID NO:) in the specification.

Claims 54-162 are pending.

Claims 54-123 and 125-131 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 11.

Claims 124 and 132-162 are examined hereinbelow.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124 and 132-162 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of a gene encoding the OB polypeptide as shown in SEQ ID NOs: 2, 4, 5 or 6 as well as any OB polypeptide thereof lacking the signal sequence of amino acids 1-21, for modulating the body weight of *ob/ob* mice or normal mice, does not

reasonably provide enablement for using other variants (except natural alleles), muteins, analogs and fragments of these OB polypeptides, nor is the specification enabling for modulating the body weight of any other mammals, including humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained essentially for reasons as set forth in the previous office action, paper No. 13, mailed 24 September 1997.

Applicant's arguments filed 27 March 1998, paper No. 16, have been fully considered but they are not persuasive. Applicant has amended claim 124 and added new claims 132-162. In regard to these claims, the following grouping are embodiments are found. Claims 124, 139, 145, and 155 contain part e) wherein a nucleic acid encoding an OB polypeptide embraces any "variants including allelic variants, muteins, analogs and fragments" of specific amino acid sequences disclosed. Claims 133, 141, 147 and 157 embrace embodiments in which the claimed nucleic acid encodes an OB polypeptide which "has 83 percent or greater amino acid sequence homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5 or 6." Claims 134, 135, 142, 143, 148, 149, 158 and 159 embrace embodiments in which the claimed nucleic acid encodes an OB polypeptide which has any or all of 22 amino acids positions substituted for another amino acid. Claim 136 is drawn to methods which embrace treating a mouse, while claim 137 is drawn to methods which embrace treating a human. The other dependent claims specify various ways in which the OB nucleic acid is delivered and expressed.

Applicant's claims will be addressed regarding two main issues. The first is in regard to the enablement of scope of the variants, muteins and analogs of the OB polypeptide embraced by the claims to have the ability to modify the body weight of a mammal. The second issue is in regard to the scope of enablement for the methods which modify the body weight of a mammal.

Applicant has included language within the claims such that the nucleic acid must encode an OB polypeptide capable of modulating body weight. This limitation may set forth a specific activity which may be determined in a functional assay, but does not enable the invention for its scope. Applicant's response at page 13 asserts that the demonstration of weight modulating activity in an animal "is a simple, reproducible and predictable means to test biological activity. Such activity is tested simply by administering to an animal a polypeptide encoded by the nucleic acids according to the present invention and measuring the weight change in that animal." Further, applicant asserts that "the present invention, by its very nature, carries with it an exceedingly accurate, simple and predictive biological assay in the form of experimental observation of changes in body weight in a test subject. The result is both quantifiable and physically observable and in Applicants [sic, Applicant's] assessment represents an ideal functional endpoint."

In response to the first issue noted hereinabove, applicant is provided the following arguments to support the examiner's position that not all variants, muteins, analogs and fragments are enabled for their scope, despite applicant's arguments to the contrary. Firstly, it is noted that

applicant has cloned the nucleic acid encoding the OB protein from two widely divergent mammalian species, mouse and human, and compared their linear arrangement of amino acids. As shown in Figure 4, it is evident that the proteins (SEQ ID NOS: 2 and 4) are highly conserved between the two. The two proteins are exactly the same length and comprise the identical amino acids in 83% of the positions (139/167 sites) when aligned 1:1. (Even within the specific amino acid sites which show divergence, nine of these sites are considered "conservative" changes by applicant. See the specification at page 12, the description of Figure 4. If such conservative changes are considered to be essentially "silent" relative to functionality in modulating body weight and are figured into calculations of similarity based upon a 1:1 comparison of the two proteins, these two proteins might be considered to be 89% identical.) This is an astounding degree of conservation, and the skilled artisan would conclude that any two proteins having such high degree of conservation across two widely divergent species of mammals must have a strict requirement for a specific arrangement of amino acids in order to function. Consequently, other than the specific amino acid sequences disclosed, it is unclear to what degree a given OB protein may diverge from either the mouse or human sequences and still retain the capability of modulating body weight as claimed. For claims that embrace muteins having substitutions or deletions of amino acids found identical between the mouse and human proteins, it is almost assured that such proteins will not be functional as claimed, absent direct evidence to the contrary. Certainly the specification provides no suggestion or evidence that any substitutions or deletions

of completely conserved amino acids would be tolerated within the limits of the claims. For substitutions within the specific sites claimed in 134, 135, 142, 143, 148, 149, 158 and 159, although there is some evidence that certain amino acids may be "conservatively" substituted and others simply substituted by another amino acid, it is not evident to what extent specific amino acid changes or combinations of changes can be tolerated and still result in an OB protein having the function claimed. Changes to a primary amino acid sequence can have effects on the folding and three dimensional structure of the protein that are simply unpredictable. As the OB protein appears to interact with specific cell-surface receptors in order to function, it is unclear what constraints on the protein are required in order for it to remain capable of an effective interaction with such receptors. Particularly as these changes may affect the degree to which this interaction occurs successfully, and the consequent cellular triggers which effect body weight modulation, such changes cannot be predicted to result in an "all-or-nothing" effect in an animal. As elaborated later, the specification does not provide for an assay which determines the degree to which a particular OB analog will modulate body weight. Thus, quantifying "modulation" may not be possible absent rigorous, statistically significant testing of a particular analog for the degree of such modulation.

Secondly, applicant's lack of enablement for the scope of the variants, muteins and analogs of the OB polypeptide as claimed is in regard to the amount of experimentation that will be needed. This point has two components. The first is in regard to the number of embodiments,

and the second is in regard to the complexity of the screening assay. As an example, claims 134, 135, 142, 143, 148, 149, 158 and 159, in which any of the twenty amino acids may be substituted at any or all of 22 specific amino acid sites, this results in a potential pool of OB analogs which numbers 20^{22} or 4.19×10^{22} possibilities. Each protein must either be synthesized, or the nucleic acid constructed, introduced into a vector, the vector introduced into a host cell and the protein expressed therein. Because the assay for activity is the ability of this protein to modulate body weight, each protein would need to be purified for testing in an animal. Alternatively, the vector may be introduced directly into the animal to be tested. Each test must be individually performed using a single specific analog in an individual animal. Assuming the skilled artisan could contemplate how to make each of these individual analogs, this would arguably constitute undue experimentation due to the sheer number needed to be made. Even then, the testing procedure is not "simple" as applicant asserts. Furthermore, as noted hereinabove, a particular analog may not exert an all-or-nothing effect on body weight of a given animal, but may cause some degree of weight change. Such changes will likely need to be quantified using statistically significant numbers of test animals to determine whether or not modulation is indeed occurring, and to what degree.

Applicant is reminded of the findings in *Amgen Inc. v. Chugai Pharmaceutical Co. Inc.* 18 USPQ2d 1016, 1026 (CAFC 1991) which addressed a similar issue of enablement and undue experimentation for analogs of the erythropoietin (EPO) gene broadly claimed and narrowly

disclosed. In that instance, it was found:

> that over 3,600 different EPO analogs can be made by substituting at only a single amino acid position, and over a million different analogs can be made by substituting three amino acids. The patent indicates that it embraces means for preparation of "numerous" polypeptide analogs of EPO. Thus, the number of claimed DNA encoding sequences that can produce an EPO-like product is potentially enormous.

Further, at page 1027, the CAFC found that:

> it is not necessary that a patent applicant test all the embodiments of his invention,...what is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought. Amgen has not done that here. In addition, it is not necessary that a court review all of the *Wands* factors to find a disclosure enabling. They are not illustrative, not mandatory. What is relevant depends on the facts, and the facts here are that Amgen has not enabled preparation of DNA sequences sufficient to support its all-encompassing claims...Here, however, despite extensive statements in the specification concerning all the analogs of the EPO gene that can be made, there is little enabling disclosure of particular analogs and how to make them. Details for preparing only a few EPO analog genes are disclosed. Amgen argues that this is sufficient to support its claims; we disagree. This "disclosure' might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO analogs. There may be many other genetic sequences that code for EPO-Type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them...[W]e do not intend to imply that genetic sequences cannot be valid where they are of a scope appropriate to the invention disclosed by an applicant. That is not the case here, where Amgen has claimed every possible analog of a gene containing about 4,000 nucleotides, with a disclosure only of how to make EPO and a very few analogs.

Finally, at page 1028, the CAFC concludes:

> Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with an attendant uncertainty as to what utility will be possessed by these analogs, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity. Under the circumstances, we find no error in the court's conclusion that the generic DNA sequence claims are invalid under Section 112.

This does not mean that applicant is not entitled to broad claims for their invention. Applicant is directed to the findings of *The Regents of The University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997). The CAFC found:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition of function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is...It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention...Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.
>
> Thus, as we have previously held, a cDNA is not defined or described by the mere

> name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a ***representative number*** of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus...This is analogous to enablement of a genus under § 112, ¶ 1, by showing the enablement of a ***representative number of species within the genus***...Mention of representative compounds encompassed by generic claim language clearly is not required by § 112 or any other provision of the statute. But, where no explicit description of a generic invention is to be found in the specification... mention of ***representative compounds*** may provide an implicit description upon which to base generic claim language... (emphasis added)

In finding the claims of '525 patent invalid in the decision in *The Regents of The University of California v. Eli Lilly and Co.*, the CAFC held:

> We will not speculate in what other ways a broad genus of genetic material may be properly described, but it is clear to us, as it was to the district court, that the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

The instant application distinguishes over the decision in *The Regents of The University of California v. Eli Lilly and Co.* in that applicant has cloned the cDNA which encodes a functional OB protein from both mouse and human. A 1:1 alignment of the two protein sequences demonstrates a very high degree of conservation at most of the amino acid sites between the two protein. Given the fact that these two mammalian cDNAs are derived from widely divergent mammalian species, it is reasonable to conclude that applicant has enabled a broad claim drawn to the genus of mammalian nucleic acids which encode the OB protein capable of modulating body

weight in a mammal, i.e. naturally occurring allelic variants. The results presented in Figure 16, as described at page 102 of the specification, demonstrates that an OB gene specific probe identified an OB gene present in DNA from a variety of mammalian species. However, beyond naturally occurring OB allelic variants, it is unclear what other muteins, analogs or fragments would function as claimed.

The second issue in regard to enablement for the scope of the invention concerns the scope of the methods which modify the body weight of a mammal. This was raised in the previous office action and is still considered valid. Applicant's response beginning at page 14 only acknowledges what was discussed in the previous office action and suggests that "it would not constitute undue experimentation to make and test OB polypeptides for use in gene therapy methods of modifying body weight in humans." The issue regarding the scope of enablement for making and using OB "variants" as broadly claimed for treating *any* mammal has been discussed thoroughly hereinabove. Therefore, for the sake of argument, the following discussion will assume that if humans are to be treated in order to modify body weight, the human OB gene allelic variant of the disclosure would be used. It is clear from the teachings of the Muzzin et al. reference, cited in the previous office action, that administration of a vector containing the leptin protein will cause a "total correction of the obese phenotype of the *ob/ob* mice." It is also evident from the teachings of Campfield et al., also cited in the previous office action, that not all obese mice will respond to such treatments because the defect causing the obesity lies in a gene other

than the that encoding the OB protein. Genetically obese *db/db* mice do not respond to increased levels of leptin. Consequently, in order to expect modulation of obesity in mice, the skilled artisan would have to know the population of animals which would benefit from administration of vectors encoding the OB protein. As set forth in the previous office action, obesity in humans is a complex issue. The previous office action stated:

> Obesity in humans may result from environmental as well as genetic factors. See Sorensen et al. [Metabolism **44(9 Suppl 3):**4-6 (1995)]. Reduction of body weight in obese humans may not be as simple and straightforward as increasing leptin levels as seen in genetically defined mouse models. See Ferrell [Human Biology **65(6):**967-975 (1993)] at page 973, first full paragraph and Lindpaintner [The New England Journal of Medicine **332(10):**679-680 (1995)], at page 680, second column, last paragraph. Finally, the teachings of Maffei et al. [Diabetes **45:**679-682 (1996)] states that defects in the OB coding region "are not a common cause of obesity in humans." See page 681, second column under DISCUSSION. It is unclear whether most individuals who are obese are so due to defects in the regulatory regions of the OB gene or for some other unrelated reason.

Because the specification fails to identify the individuals within the population of obese humans who would benefit from administration of a vector encoding the OB protein, the invention cannot be said to be enabled for modulating body weight as broadly claimed. The teachings of Maffei et al. seem to indicate that defects in the *ob* gene coding region in humans does not appear to be a common cause of obesity in humans. Therefore, absent evidence to the contrary, it is unclear if increased expression of the OB protein within a given obese human would have the intended effect of modulating body weight of that individual. Given the lack of guidance of the specification on how to affect body weight changes in humans, the uncertainty in the state of the

art as to the complex causes of obesity in humans, the unpredictability of gene therapeutics in general in the art and the lack of any current art recognized genetic alterations of body weight in humans, it would require undue experimentation to practice the invention for its scope. Even if applicant has evidence that *ob/ob* human individuals can be identified, and it can be demonstrated that such individuals can benefit directly from administration of vectors expressing the OB protein, the scope of the invention would at least have to be limited to those individuals which are specifically identified with the *ob/ob* genotype. Regarding evidence that normal mice show weight loss when administered the OB protein, it is noted that this is not commensurate with what is being claimed. The claims are drawn to treatments with vectors expressing the OB protein. It is unclear what effects administration of such vectors would have in either "normal" weight mice or "normal" weight humans. The effects of unregulated OB protein expression in an individual, whether human or mouse, cannot be predicted and the specification does not set forth conditions for how to use vectors for controlled, specific and regulated expression of the OB protein. If applicant wishes to pursue claims drawn to the treatments using the OB protein alone, independent of administration of vectors expressing the OB protein, such claims would be considered a drawn to an independent and distinct invention. Such claims would be subject to a restriction requirement.

Claims 133, 141, 147 and 157 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

For claims 133, 141, 147 and 157, applicant has introduced new claims which contain the language "...wherein said OB polypeptide has 83 percent or greater amino acid homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5 or 6." There is no support in the specification for the percent homology. The mouse and human proteins of SEQ ID NOS: 2 and 4 are exactly the same length when compared to each other. The mouse and human proteins of SEQ ID NOS: 5 and 6 are exactly the same length when compared to each other. When the amino acid residues of SEQ ID NOS: 2 and 4 are aligned exactly 1:1, there are identical amino acids at 139 of 167 sites. When the amino acid residues of SEQ ID NOS: 5 and 6 are aligned exactly 1:1, there are identical amino acids at 139 of 166 sites. This amounts, respectively, to 83.2% and 83.7% of the amino acid residues being identical and in exactly the same position when these two sets of mouse and human proteins are compared. Note Figure 4, for example. There is no teaching in the specification of OB proteins described generally as having homology in terms of 83% or greater to any of these SEQ ID NOS. The term" 83% or greater...homology" appears to have been added by applicant to the new claims and has no direct support in the specification as filed.

Claims 161 and 162 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 161 and 162 are drawn to methods in which the either the expression of the endogenous OB protein is activated by a homologous recombinational event which inserts an "expression regulatory sequence in functional proximity to the OB polypeptide encoding sequence" either directly in cells within the animal or in cells *in vitro,* which cells are then administered to the animal. It first must be noted that all of the claims require a recombinational event within the claimed host cell in order to insert some sort of "expression regulatory sequence in functional proximity to the OB polypeptide encoding sequence." What this is interpreted to mean is that the "expression regulatory sequence" is introduced into the host cell such that it will recombine with the OB gene sequences present within the host cell chromosome and substitute for the resident expression regulatory sequences. The result would be that the OB gene present within the host chromosome would now fall under the expression regulation of these newly introduced sequences. In order for this to occur, it would require the skilled artisan to identify the resident OB regulatory sequences such that a nucleic acid construct could be generated which contained regions of homology with that OB regulatory sequence to allow for recombination within the chromosome. It is crucial to know the identity of the OB upstream sequences in order to design proper nucleic acid constructs for recombination in order to express the OB gene present in the chromosome. Applicant's specification is prophetic in its hope that such sequences can be

identified by the skilled artisan. The specification fails to describe how to obtain any of these DNA sequences and fails to describe them so that the invention can be made and used as claimed. Applicant is again directed to the decisions in *Amgen Inc. v. Chugai Pharmaceutical Co. Inc.* 18 USPQ2d 1016, 1026 (CAFC 1991) and *The Regents of The University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) regarding adequate description of gene sequences, rather than relying simply upon an indication of what that gene does for enablement. Finally, applicant is directed to review the U.S. Patent 5,698,389 which does teach the promoter of the mouse OB gene. Nowhere in applicant's specification are these regulatory sequences predicted, taught or described.

Claim 124, 133, 141, 147 and 157 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 124, the method involves "administering a nucleic acid". The composition of this nucleic acid is unclear. The specification discusses including the OB gene in vectors for delivery to cells *ex vivo* or directly *in vivo*. Other than administration of vectors comprising the OB gene, it is unclear what is the composition of this nucleic acid as claimed for administering to the mammal. Applicant has failed to address this rejection in their response. Simply because a nucleic acid is "capable" of modulating body weight" as claimed does not set forth with any particularity how that protein is delivered and expressed. Without proper elements

for expression, and those elements clearly set forth in the claim, claim 124 is incomplete. Compare this claim to claim 144, for example.

Regarding claims 133, 141, 147 and 157, the specification fails to set forth the meaning of the term "homology" as claimed and how applicant arrived at the percentage. Homology of a nucleic acid sequence requires the comparison of two sequences using a computer algorithm which accounts for alignment, including potential gaps in that alignment. The parameters of the algorithm may be set to account for conservative substitutions of amino acid sequences. As noted hereinabove, applicant appears to have arrived at the term 83 percent based upon a comparison of two specific amino acid sequences in which the two sequences are of identical length, include no gaps in the alignment and provide for no inclusion of conservative changes within the calculations. See Figure 4, for example. The claims do not set forth with any particularity how the percentage is calculated and the basis for that calculation. Consequently, the claims are vague and indefinite.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Art Unit 1636 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for Art Unit 1636 is (703) 308-4242 or 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. F. Railey, whose telephone number is (703) 308-0281. The examiner can normally be reached on Monday-Thursday, and alternate Fridays, from 8:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

George Elliott, can be reached at (703) 308-4003. The fax phone number for informal transmissions to the examiner is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

17 May 1998

JOHNNY F. RAILEY II, PH.D.
PRIMARY EXAMINER
GROUP 1630